PATENT
Docket No. 220.00010150

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Eric T. Kool	Group Art Unit:	1635
Serial No.:	09/997,931	Examiner:	S. McGarry
Confirmation No.:	5355		
Filed:	November 30, 2001		

#9

For: CIRCULAR DNA VECTORS FOR SYNTHESIS OF RNA AND DNA

Patent Application Publication No.: US 2003/0087241 A1

REQUEST FOR CORRECTION OF PATENT APPLICATION PUBLICATION

Mail Stop PGPub
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This paper is a request for correction and republication of the above-identified Patent Application Publication, which was published on May 8, 2003.

Applicant's Representatives identified the following errors made by the U.S. Patent and Trademark Office: On page 55, claim 85, line 57, the line reads, "to 104 nucleotides.", it should read, "to 10^4 nucleotides.". This is evidenced by page 103, claim 85, line 14 of the originally filed application.

Also on page 56, claim 90, line 7, please replace "delectably" with "detectably". This is evidenced by page 103, claim 90, line 30 of the originally filed application.

The errors are indicated on the form entitled "Errors on Published Application" included herewith. A copy of the patent application publication with errors marked is also included herewith.

Pursuant to 37 C.F.R. § 1.221(b), we request that the errors indicated above be corrected, and that the above-identified Patent Application Publication be re-published without additional publication or processing fees.

CERTIFICATE UNDER 37 C.F.R. 1.8:

The undersigned hereby certifies that this paper is being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Mail Stop PGPub, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 28th day of May, 2003, at 10:20am (Central Time).

Name: Sara E. Olson

28 May 2003
Date

Respectfully submitted for
University of Rochester

By
Mueting, Raasch & Gebhardt, P.A.
P.O. Box 581415
Minneapolis, MN 55458-1415
Phone: (612)305-1220
Facsimile: (612)305-1228
Customer Number 26813

26813
PATENT TRADEMARK OFFICE

By:
Victoria A. Sandberg
Reg. No. 41,287
Direct Dial (612)305-1226

Errors on Published Application

File No. 220.00010150 Inventor: Eric T. Kool

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Published Application Claim #	Page/Line #	Application as Filed Claim #	Page/ Line #	Error Fault	Correction
85	Pg. 55/ Line 57	85	Pg. 103/ Line 14	PTO	"104" should be "10^4"
90	Pg. 56/ Line 7	90	Pg. 103/ Line 30	PTO	"delectably" should be "detectably"

51. The biologically active RNA oligonucleotide of claim 50 comprising a ribozyme.

52. A method for synthesizing an RNA oligonucleotide comprising contacting the cell of a living organism in situ with a single-stranded circular oligonucleotide template comprising at least one copy of a nucleotide sequence complementary to the sequence of the desired RNA oligonucleotide, such that the circular oligonucleotide is taken up by the cell and processed intracellularly to yield an RNA oligonucleotide multimer comprising multiple copies of the desired RNA oligonucleotide.

53. The method of claim 52 wherein the circular oligonucleotide has about 15-1500 nucleotides.

54. The method of claim 52 wherein the living organism is a plant or an animal.

55. The method of claim 52 wherein the living organism is a human.

56. The method of claim 52 wherein the RNA oligonucleotide multimer is cleaved to yield multiple copies of the desired RNA oligonucleotide.

57. The method of claim 56 wherein the cleavage is autolytic.

58. The method of claim 56 wherein the desired RNA oligonucleotide is linear.

59. The method of claim 56 wherein the desired RNA oligonucleotide is circular.

60. The method of claim 52 or 56 wherein the desired RNA oligonucleotide is biologically active.

61. The method of claim 60 wherein the biologically active RNA oligonucleotide comprises a catalytic RNA, an antisense RNA, or a decoy RNA.

62. The method of claim 60 wherein the desired oligonucleotide has endonuclease, exonuclease, polymerase, ligase, phosphorylase, dephosphorylase, or protease activity.

63. The method of claim 60 wherein the desired oligonucleotide comprises a ribozyme.

64. The method of claim 63 wherein the ribozyme is a hairpin, hammerhead-motif, or hepatitis delta catalytic ribozyme.

65. The method of claim 60 wherein the biologically active RNA oligonucleotide is capable of intramolecular ligation.

66. The method of claim 65 wherein the biologically active RNA oligonucleotide comprises a hairpin-type ribozyme.

67. The method of claim 63 wherein the desired RNA oligonucleotide is capable of trans cleavage.

68. The method of claim 63 wherein the desired RNA oligonucleotide cleaves a target disease-associated RNA, DNA, or protein.

69. The method of claim 52 or 56 wherein the circular oligonucleotide is administered to the organism using direct injection, inhalation, intranasal administration, ocular administration, site-specific incubation or infusion.

70. The method of claim 69 wherein the circular oligonucleotide is administered via direct injection.

71. The method of claim 70 wherein the organism is a mammal and wherein the circular oligonucleotide is administered to the mammal subcutaneously, intramuscularly, or intravenously.

72. The method of claim 69 wherein a gene encoding an effective RNA polymerase operably linked to a promoter is co-introduced into the cell.

73. The method of claim 72 wherein the gene encoding an effective RNA polymerase is administered to the mammal via direct injection.

74. The method of claim 72 wherein the RNA polymerase is T7 or E. Coli polymerase.

75. The method of claim 52 or 56 wherein the desired RNA oligonucleotide modifies the structure or the function of a target disease-associated DNA, RNA, or protein.

76. The method of claim 75 wherein the desired RNA oligonucleotide comprises a biologically active RNA that cleaves a target disease-associated RNA in trans.

77. A method for treating disease in a living organism comprising administering to the organism an RNA oligonucleotide multimer synthesized according to the method of claim 1, wherein the RNA oligonucleotide multimer modifies the structure or function of a target disease-associated molecule.

78. A method for treating disease in a living organism comprising administering to the organism an RNA oligonucleotide synthesized according to the method of claim 16, wherein the RNA oligonucleotide modifies the structure or function of a target disease-associated molecule.

79. The method of claims 77 or 78 wherein the target disease-associated molecule comprises a nucleic acid.

80. The method of claim 79 wherein the target disease-associated nucleic acid is RNA.

81. The method of claim 80 wherein the desired oligonucleotide comprises a biologically active RNA that cleaves a target disease-associated RNA in trans.

82. An RNA molecular weight standard kit comprising packaging containing, separately packaged, a population of about 4-50 repeating unit RNA molecules each having a different number of nucleotides such that each successively larger repeating unit RNA molecule differs from the immediately preceding repeating unit RNA molecule by a number of nucleotides equal to the number of nucleotides in a single-stranded circular oligonucleotide template; wherein the circular oligonucleotide template comprises at least one copy of a nucleotide sequence that encodes a ribozyme and a cleavage site for the ribozyme; and wherein the population of repeating unit RNA molecules is synthesized by contacting the circular oligonucleotide template with an effective RNA polymerase and an effective amount of at least two ribonucleotide triphosphates to yield an RNA oligonucleotide multimer, for a period of time effective to allow partial autolytic cleavage of the RNA oligonucleotide multimer to yield the desired population of repeating unit RNA molecules.

83. The RNA molecular weight standard kit of claim 82 wherein the circular oligonucleotide template has about 15 to 1500 nucleotides.

84. The RNA molecular weight standard kit of claim 83 wherein the circular oligonucleotide template has about 20 to 500 nucleotides.

85. The RNA molecular weight standard kit of claim 82 wherein the RNA molecules range in length from about 50 to 10~~4~~ nucleotides. 10⁴

86. The RNA molecular weight standard kit of claim 85 wherein the RNA molecules range in length from about 50 to 500 nucleotides.

87. The RNA molecular weight standard kit of claim 82 wherein the population of RNA molecules comprises a lyophilized powder.

88. The RNA molecular weight standard kit of claim 82 wherein the population of RNA molecules comprises a buffered solution containing a quenching agent.

89. The RNA molecular weight standard kit of claim 88 wherein the quenching agent is formamide, urea, or EDTA.

detectably

90. The RNA molecular weight standard kit of claim 82 wherein the RNA molecules are ~~detectably~~ labeled.

91. A kit for synthesizing RNA molecular weight standards comprising packaging containing, separately packaged, instructions for use and a single stranded circular oligonucleotide template comprising at least one copy of a nucleotide sequence that encodes a ribozyme and a cleavage site for the ribozyme.

92. The kit of claim 91 wherein the circular oligonucleotide template has about 15-1500 nucleotides.

93. The kit of claim 92 wherein the circular oligonucleotide template has about 20-500 nucleotides.

94. The kit of claim 91 wherein the circular oligonucleotide template is devoid of an RNA polymerase promoter.

95. A method for synthesizing an RNA oligonucleotide inside a cell comprising introducing into a cell a single-stranded circular oligonucleotide template comprising at least one copy of a nucleotide sequence complementary to the sequence of the RNA oligonucleotide, such that the circular oligonucleotide is processed intracellularly to yield an RNA oligonucleotide multimer comprising multiple copies of the RNA oligonucleotide.

96. The method of claim 95 wherein the circular oligonucleotide has about 15-1500 nucleotides.

97. The method of claim 95 wherein the cell is a plant cell or an animal cell.

98. The method of claim 95 wherein the cell is a bacterial cell.

99. The method of claim 95 wherein the cell is a mammalian cell.

100. The method of claim 95 further comprising cleaving the RNA oligonucleotide multimer to yield multiple copies of the RNA oligonucleotide.

101. The method of claim 100 wherein the cleavage is autolytic.

102. The method of claim 100 wherein the RNA oligonucleotide is linear.

103. The method of claim 100 wherein the RNA oligonucleotide is circular.

104. The method of claim 100 wherein the RNA oligonucleotide is biologically active.

105. The method of claim 104 wherein the biologically active RNA oligonucleotide comprises a catalytic RNA, an antisense RNA, or a decoy RNA.

106. The method of claim 104 wherein the biologically active RNA oligonucleotide has endonuclease, exonuclease, polymerase, ligase, phosphorylase, dephosphorylase, or protease activity.

107. The method of claim 104 wherein the biologically active RNA oligonucleotide is capable of intramolecular ligation.

108. The method of claim 104 wherein the biologically active oligonucleotide comprises a ribozyme.

109. The method of claim 108 wherein the ribozyme is a hairpin, hammerhead-motif, or hepatitis delta catalytic ribozyme.

110. The method of claim 108 wherein the ribozyme is capable of trans cleavage.

111. The method of claim 108 wherein the ribozyme cleaves a target disease-associated RNA, DNA, or protein.

112. The method of claim 104 wherein the biologically active RNA oligonucleotide modifies the structure or the function of a target disease-associated DNA, RNA, or protein.

113. The method of claim 95 wherein a gene encoding an effective RNA polymerase operably linked to a promoter is co-introduced into the cell.

114. The method of claim 113 wherein the RNA polymerase is T7 or *E. coli* polymerase.

115. The method of claim 95 wherein the circular oligonucleotide template is introduced into the cell using direct injection, electroporation, heat shock, calcium phosphate treatment, lipid-mediated delivery, or cation-mediated delivery.

116. The method of claim 95 further comprising implanting the cell into a plant or animal after introducing the single-stranded circular oligonucleotide template into the cell.

117. The method of claim 95 performed in a cell explanted from a plant or animal.

118. The method of claim 117 further comprising implanting the cell into a plant or animal after introducing the single-stranded circular oligonucleotide template into the cell.

119. The method of claim 118 wherein the cell is reimplanted into the plant or animal from which it was explanted.

120. The method of claim 117 wherein the animal is a mammal.

121. The method of claim 95 performed in cell culture.

122. The method of claim 95 performed in situ in a living organism.

123. The method of claim 122 wherein the circular oligonucleotide is administered to the organism using direct injection, inhalation, intranasal administration, ocular administration, site-specific incubation or infusion.

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X **Small Entity Status is entitled to be asserted in the above-identified application.**

Please consider this a PETITION FOR EXTENSION OF TIME for a sufficient number of months to enter these papers and please charge any additional fees or credit overpayment to Deposit Account No. 13-4895.

28 May 2003
Date

Mueting, Raasch & Gebhardt, P.A.
Customer Number: 26813

26813
PATENT TRADEMARK OFFICE

By: Victoria A. Sandberg
Victoria A. Sandberg
Reg. No. 41,287
Direct Dial (612)305-1226

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May 28, 2003
Date

Signature: Sara E. Olson
Name: Sara E. OLSON

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